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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,962	06/25/2001	STEPHEN PHILIP JACKSON	MEWE-010	5713

24353 7590 05/06/2004

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) before the application can be examined under 35 U.S.C. 131 and 132.

APPLICANT IS GIVEN 3 MONTHS FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for response beyond the SIX MONTH statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The Examiner can normally be reached daily from 9:00 A.M. to 6:00 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Christopher S.F. Low, can be reached at (703) 308-2923. The OFFICIAL fax phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

A reply to a notice to comply with the sequence rules should not be sent to the 20231 zip code address for the United States Patent and Trademark Office.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual-ePAVE)

2. Mailed to:
Commissioner for Patents
P.O. Box 22313-1450

Alexandria, VA 22313-1450

3. Hand Carried directly to:
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Technology Center 1600, Reception Area 7th Floor
Examiner Hope Robinson
Sequence Information
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Arlington, VA 22202

4. Hand Carried directly to the Customer Window at:
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Office Action Summary	Application No.	Applicant(s)	
	09/462,962	JACKSON ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I (claims 1-11, 13-15 and 17-18) is acknowledged.

Claim Disposition

2. Claims 1-29 have been canceled. Claims 30-35 have been added. Claims 30-35 are pending and under examination.

Specification

3. The specification is objected to because of the following informalities:

The specification is objected to because on page 1 there is no mention of the priority information, for example, that this application is a 371. In addition, sequences are disclosed for example on page 24, however, no sequence notation is provided, for example, SEQ ID NO:. Further, on page 55, line 1 the word "modulate" is misspelled as "modlate". The specification provides Figures such as Figs. 6, 7, 8 and 9 which have item (b) that consists of parts (ii), however are not described as such (see page 19). For example Figure 6(b) has parts (ii) through (vii) and these are not described in the "Brief Description of the Drawings.

In addition it is noted that applicant did not provide a computer readable for the sequence. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) before the application can be examined under 35 U.S.C. 131 and 132.

Correction of the above and compliance with the sequence rules is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to an assay method for a compound able to modulate the interaction between (i) ATM or

ATR and (ii) p53, the method including the steps of: (a) bringing into contact a substance including a peptide fragment of (i) or a derivative, variant or analogue thereof, a substance including the relevant fragment of p53, or a variant, derivative or analogue thereof, and a test compound; and (b) determining interaction or binding between said substances and test compound. Note that the preamble is missing a description of whether the assay is to "detect a compound", "identify a compound" or "screen for a compound". Furthermore, the specification does not provide a compound that was identified using the above assay method to demonstrate the claimed invention. The specification on pages 51+ state that the compound or agent can be a "peptide, antibody, small molecule, or mimetic", however, no such compound is identified. In addition, the method does not set forth the type of interaction of ATM or ATR with p53. Is this a direct interaction or indirect? As step (b) recites "determining interaction or binding" it appears that the interaction is not one of binding and it is unclear what part of ATM or p53 interacts, for example what sites, regions or domains. Depending on the type of interaction and the site of interaction or binding between the two proteins, the compound might not affect the binding or interaction or derivatives of the proteins. Thus, adequate written description of the claimed invention is necessary to allow one of skill in the art to be able to practice the invention as claimed without undue experimentation.

Step (a) of the method is bringing into contact a substance including a peptide fragment of ATM or ATR, however, it is unclear what substance is being contacted or other components are included as the only requirement is that it includes a

fragment/derivative/analogue of ATM or ATR (see for example claim 30). Additionally, there is no indication as to whether a derivative, analogue, variant or fragment of ATM, ATR or p53 will have the same interaction or bind; or if said compound will have an effect on the interaction. Additionally, the instant method does not have a step to separate or detect the compound sought. Moreover, the claims do not set forth whether modulate in the preamble of the claims refers to a positive or negative effect/change. Note that the claims recite, "modulate the interaction" and it is unclear if this will result in activation or inhibition/disruption or activation of the interaction, essentially, is this a positive or negative change to the interaction between p53 and ATM or ATR?

In addition the claims are directed to a fragment, derivative, variant or analogues thereof, of the claimed ATM or ATR, however, neither the claim nor the instant specification describes said fragment/variant/derivative/analogue. The specification does not define when a protein ceases to be a variant/fragment etc. of the claimed protein. Thus, the claims are directed to a genus of proteins to which neither the specification or claims indicate what distinguishing attributes are shared by the members of the genus. The specification and claim do not place any limit on the number of variations that can occur to the claimed protein. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. An assay method for a compound that modulates the interaction between ATM or ATR and p53 which involves

an unknown substance that includes a variant/fragment/derivative/analogue of ATM or ATR that does not have a defined structure or function, requires undue experimentation to determine if once a fragment is constructed it would inhibit or stimulate the interaction or have no effect.

Thus, applicant was not in possession of the claimed genus. Therefore, for all these reasons the invention has not been adequately described in the specification and would require undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30, item (b) lacks antecedent basis for "said substances and test compound" as item (a) recites "substance and test compound". In addition, the recitation of "determining interaction or binding" in item(b) lacks antecedent basis as the preamble of the claim recites "interaction". The claim is also indefinite as the preamble is confusing where it recites " an assay method for a compound able to modulate the interaction between ATM or ATR and p53", the claim does not state that it is a method to screen for compounds or to identify compounds or to detect compounds.

Claims 30-35 are indefinite because the mere recitation of ATM or ATR is insufficient to convey what applicant intends to be the claimed invention, the spelled out meaning of the acronym should be recited in the claim, for example, it is known in the art that "atm" is an abbreviation for atmosphere. The acronyms could also represent the tripeptides: Ala-Thr-Arg and Ala-Thr-Met. In addition, the claims are indefinite for the recitation of "modulate" as this term could mean inhibit or activate, upward or downward and there is no indication in the claim as to whether the assay method to obtain a compound to affect the interaction is going to have a positive or negative effect.

Claim 31 is indefinite because the claimed method preamble is "an assay method for a compound able to modulate" which is being interpreted as the identification of a compound, and the end result of the method is "determining phosphorylation at said site" which does not indicate that said compound was obtained or identified. There is no nexus between the preamble of the claim and the end point.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

7. Claims 30, 32, 33 and 35 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Hoekstra et al. (WO 97/18323, May 22, 1997) in view of Jongmans et al. (Oncogene, vol. 13, page 1133-1138, 1996).

Hoekstra et al. teach an assay for identifying modulators of ATM (identified as the cell cycle checkpoint phosphatidylinositol kinase related protein) and MCSS1 gene which is similar to p53 that involves contact with a test compound and a determination/quantification step (claims 30 and 32; see abstract, page 11 and claim 26 of the reference). Hoekstra et al. state that if a particular form of cancer results from a mutation in a gene such at p53 (claim35), an agent which inhibits the transcription or the enzymatic activity may be used to render cancerous cells more sensitive to chemotherapy or radiation therapy (page 11). In-so-far-as Hoekstra et al. does not explicitly teach the modulation of the interaction between ATM and p53 (claim 33), Jongmans teach that the ATM gene is upstream of p53 in a signal transduction pathway

which activates multiple cellular pathways in response to DNA damage produced by ionizing radiation. As it is well known in the art that ATM is part of a pathway that responds to DNA damage from ionizing radiation, thus ATM selectively regulates distinct p53-dependent cell cycle checkpoint and apoptotic pathways, a compound that modulates ATM will affect the interaction of ATM with p53.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Hoekstra et al. and include that modulation of ATM affects the interaction between ATM and p53 because Jongmans state that ATM is upstream of p53 in a signal transduction pathway which activates multiple cellular pathways in response to DNA damage, thus inhibiting ATM would therefore affect the interaction between p53 and ATM. The skilled artisan would therefore, be motivated to add in the effect that modulating ATM affects the interaction of ATM with p53, because Hoekstra et al. disclose an assay method to identify compounds that modulate ATM and agents that would modulate genes such as p53, stating that the therapeutic value in such an agent lies in the fact that current radiation therapy or chemotherapy does nothing to overcome the ability of the p53 mutant cancerous cell to sense and correct the DNA damage imposed as a result of the treatment. Furthermore, Jongmans state that p53 induction is significantly reduced following exposure to ionizing radiation in AT cell lines (see page 1133) which demonstrates the need for said compound.

Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

Conclusion

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

Hope A. Robinson, MS

Patent Examiner

Application No.: 09/462,962

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or
1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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